The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte RUSSELL M. MEDFORD and CLARENCE F. BENNETT

_____

Appeal No. 1997-4380
Application No. 08/147,878

_____

ON BRIEF

_____

Before WINTERS, ADAMS, and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL[1]

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2, 5, 8, 15-17 and 34, which are all the claims pending in the application.

[1] We recognize appellants' request (Paper No. 26, received August 28, 1997) for oral hearing in this appeal. However, in our review of this appeal we find a hearing unnecessary. 37 CFR § 1.194(c). Accordingly, we make our decision on brief.

Claims 1 and 34 are illustrative of the subject matter on appeal and are reproduced below:

1. A method for modulating expression of a gene coding for a vascular cell adhesion molecule selected from the group consisting of VCAM-1, ICAM-1 and E-selectin comprising contacting cells with an oligonucleotide moiety consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

34. An oligonucleotide moiety consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

The references relied upon by the examiner are:

Bielinska et al. (Bielinska), "Regulation of gene expression with double-stranded phoshorothioate oligonucleotides," Science, Vol. 250, pp. 997-1000 (1990)

Baeuerle, "The inducible transcription activator NF-κB: regulation by distinct protein subunits," Biochimica et Biophysica Acta, Vol. 1072, pp. 63-80 (1991)

Degitz et al. (Degitz), "Cloning and characterization of the 5' transcriptional regulatory region of th ehuman intercellular adhesion molecule 1 gene," J. Biol. Chem., Vol. 266, No. 21, pp. 14024-14030 (1991)

Montgomery et al. (Montgomery), "Activation of endothelial-leukocyte adhesion molecule 1 (ELAM-1) gene transcription," Proc. Natl. Acad. Sci. U.S.A., Vol. 88, pp. 6523-6527 (1991)

Iademarco et al. (Iademarco), "Characterization of the promoter for vascular cell adhesion molecule-1 (VCAM-1)," J. Biol. Sci., Vol. 267, No. 23, pp. 16323-16329 (1992)

Miller et al. (Miller), "Gene transfer and antisense nucleic acid techniques," Parasitology Today, Vol. 10, No. 3, pp. 92-97 (1994)

Wagner, "Gene inhibition using antisense oligodeoxynucleotides," Nature, Vol. 372, pp. 333-335 (1994)

Wu-Pong, "Oligonucleotides: opportunities for drug therapy and research," Pharmaceutical Technology, Vol. 18, pp. 102-114 (1994)

Stull et al. (Stull), "Antigene, ribozyme and aptamer nucleic acid drugs: progress and prospects," Pharmaceutical Research, Vol. 12, No. 4, pp. 465-483 (1995)

GROUNDS OF REJECTION

Claims 1, 2, 5, 8 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claims.

Claims 1, 2, 15-17 and 34 are rejected under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Iademarco.

Claims 1, 5, 15 and 16 are rejected under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Degitz.

Claims 1, 8, 15 and 16 are rejected under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Montgomery.

We reverse the rejections under 35 U.S.C. § 103. We vacate the rejection under 35 U.S.C. § 112, first paragraph and remand this application to the examiner to reevaluate his enablement issues under the proper legal standards.

DISCUSSION

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer[2] for the examiner's reasoning in support of the rejection. We

[2] Paper No. 23, mailed June 27, 1997.

further reference appellants' Brief[3], and appellants' Reply Brief[4] for the appellants' arguments in favor of patentability.

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 370 (CCPA 1971). See also, In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988):

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in In re Forman, [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (footnote omitted).

In this case the examiner failed to analyze the claimed invention with reference to the factors set forth in Wands. Instead the examiner merely makes a series of conclusions:

> The specification does not adequately teach how to deliver the claimed oligonucleotides (oligos) *in vivo*. [Answer, page 5]…. The specification does not adequately teach how to use the claimed methods *in vivo* because it does not disclose what happens when the oligos are administered. [Answer, page 6]…. The specification does not explain how to use the claimed methods for diagnosis. [Answer, page 7].

[3] Paper No. 22, received March 31, 1997.
[4] Paper No. 25, received August 28, 1997.

Then the examiner cites Wagner, Stull, Wu-Pong and Miller to support his conclusion (Answer, page 5) that "[a]t the time the application was filed, this [delivery of oligonucleotides in vivo] was not a trivial matter." Appellants argue (Brief, page 6) that "[a]pplicants provide numerous examples in the 'Background of the Invention' section of the application in which oligonucleotides have been used *in vivo*" citing a number of PCT references. In response the examiner simply concludes without reasoned analysis that (Answer, page 11) without reasoned analysis that:

> Appellants cite a number of published PCT applications which allegedly show that oligos can be used *in vivo*. This argument is not persuasive because the review articles cited by the [e]xaminer were all published more recently. These reviews clearly indicate that *in vivo* use of oligos required more than routine experimentation at the time the application was filed.

We are not persuaded that the examiner met his burden merely because the references he cites where published closer to the date the application was examined than the date of invention, or the date of those references presented in appellants' specification in support of enablement. We remind the examiner that:

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure [emphasis added].

In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 370 (CCPA 1971). See also In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (CAFC 1993) (the PTO

bears an initial burden of setting forth a reasonable explaination … this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement). On this record, we find no fact based explanation as to why the examiner doubts the assertions made in the specification, and relied upon by appellants.

Furthermore, the examiner relies upon Miller, Wagner and Wu-Pong each published in 1994, and Stull published in 1995, to support his lack of enablement rejection. We remind the examiner, as set forth in Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1371 (Fed. Cir. 1999) "[w]hether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, *see Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986)."

With regard to the examiner's reference to Baeuerle and related concern regarding the activation of transcription by NF-κB (Answer, bridging paragraph, apges 6-7), appellants argue (Brief, page 7) that "[t]he concerns recited in the Answer are directed to the safety and side effects of the claimed method; they are best left to the Food & Drug Administration, not the PTO." We agree with appellants. See In re Anthony, 414 F.2d 1383, 1395, 162 USPQ 594, 604 (CCPA 1969)("Congress has given the responsibility to the FDA, not to the [PTO], to determine . . . whether drugs are sufficiently safe").

Accordingly, we vacate the rejection of claims 1, 2, 5, 8 and 15-17 under 35 U.S.C. § 112, first paragraph and we remand the application to allow the examiner

an opportunity to reevaluate the issue of enablement in view of the correct legal standards. In reconsidering the issue of enablement, we recommend that the examiner review Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371, 52 USPQ2d 1129 1371 (Fed. Cir 1999). Therein, the court provided a model analysis of enablement issues and illustrates the type of fact finding which is needed before one is in a proper position to determine whether a given claim is enabled or non-enabled.

THE REJECTIONS UNDER 35 U.S.C. § 103:

In each of the three sets of rejections under 35 U.S.C. § 103 the examiner cites Bielinska in view of either Iademarco, Degitz or Montgomery. In each statement of rejection the examiner states (Answer, pages 7, 8, and 9) that:

> "Bielinska et al. teach a method for inhibiting gene transcription in human cells by administration of double-stranded oligos having sequences of transcription factor binding sites (entire document). Bielinska et al. state that "[w]ith the method described in this report, funciton of the DNA-binding proteins themselves can be inhibited if the cis-acting regulatory elements have been characterized" (p. 999, cols. 2-3).

However, the examiner finds (Answer, pages 7, 9, and 10) that Bielinska does not teach the sequence of the human VCAM-1 promoter (claims 1, 2, 15-17 and 34), ICAM-1 promoter (claims 1, 5, 15 and 16), or E-selectin promoter (claims 1, 8, 15 ad 16).

To overcome the deficiency in Bielinska the examiner applies either Iademarco to teach (Answer, page 8) "the sequence of the human VCAM-1 promoter (Fig. 3)," Degitz to teach (Answer, page 9) "the sequence of the human ICAM-1 promoter (Fig. 2)," or Montgomery to teach (Answer, page 10) "the sequence of the promoter of the human ELAM-1 (E-selectin) gene (Fig. 2)."

Appellants argue (Brief, pages 8, 11, and 12) that each of Iademarco, Degitz and Montgomery merely teach the sequence of the promoter region of their respective adhesion molecule gene. Each of appellants claims are directed to specific sequences. The examiner argues (Answer, page 12) that:

> Appellants argue that the prior art does not suggest the nucleotide sequences of the claimed oligos. This argument is not persuasive … [t]he only element of the claimed invention which is not explicitly taught is the length of the oligos, which [a]ppellants admit is easily ascertained by one of ordinary skill in the art (specification p. 19, lines 4-7).

The examiner incorporates this argument as it applies to the rejection of claims 1, 2, 15-17 and 34 over Bielinska in view of Iademarco to the remaining two rejections under 35 U.S.C. § 103. See Answer, page 13 "[a]ppellants repeat the arguments made against the previous two rejections, which are not persuasive for the reasons discussed above." Appellants' specification page 19, lines 4-7 states "[p]ersons of ordinary skill in the art can easily ascertain optimal lengths of oligonucleotide for interaction with particular transcription factors." To the extent that the examiner relies upon appellants' statement and considers the Adiscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art,@ In re Boesch, 617 F.2d 272, 276, 205 USPQ

215, 219 (CCPA 1980) (citations omitted), our reviewing court has found an exception to this general rule where Athe parameter optimized was not recognized to be a result effective variable,@ In re Antonie, 559 F.2d 618, 621, 195 USPQ 6, 8 (CCPA 1977). On this record, absent the benefit of appellants' specification, the examiner does not identify, and we do not find, a suggestion in the prior art that the length of the nucleotide sequence is a result effective variable. Furthermore, even if there was a suggestion in the art that the length of the nucleotide sequence is a result effective variable, we do not find a suggestion in the prior art relied upon that suggests that the specific nucleotide sequences claimed by SEQ ID NO.

To the extent that the references could be combined as the examiner argues, the combination is inconsistent with the proper standard for obviousness. The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Laskowski, 871 F.2d 115, 117, 10 USPQ2d 1397, 1398-99 (Fed. Cir. 1989); In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here no reference applied by the examiner taken alone or collectively teaches the SEQ ID NO limitations of each claim on appeal. The examiner does not identify, and we do not find, a suggestion in the prior art relied upon that would indicate that the prior art should be modified to have the exact sequences in the claims.

Therefore, on this record, we are constrained to reach the conclusion that the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness. Accordingly, we reverse the rejection of claims 1, 2, 15-17 and 34 under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Iademarco. We reverse the rejection of claims 1, 5, 15 and 16 under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Degitz. We reverse the rejection of claims 1, 8, 15 and 16 under 35 U.S.C. § 103 as being unpatentable over Bielinska in view of Montgomery.

This application, by virtue of its "special" status, requires an immediate action. MPEP § 708.01(D) (7th ed., rev. 1, February 2000). It is important that the Board be informed promptly of any action affecting the appeal in this case.

REVERSED

Sherman D. Winters Administrative Patent Judge	)
Donald E. Adams Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

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Eli Lilly and Company
Patent Division JJS
Lilly Corporate Center
Indianapolis IN 46285